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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,633	04/13/2004	Markus Stoffel	1119-14	6325

23869 7590 04/17/2007
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EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,633	STOFFEL ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *1-17,55-63,66 and 67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21, 23-54, 64 and 65* is/are rejected.

7)☒ Claim(s) *22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/24/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of group III, claims 18-54, 64 and 65 and SEQ ID NO: 1 in the reply filed on 2/8/07 is acknowledged.

Claims 1-17, 55-63, 66 and 67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/8/07.

Claims 1-67 are pending in the instant application.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because there are sequences in the drawings, for example, that do not contain a SEQ ID NO.

A complete response to this office action must correct the defects cited above regarding compliance with the sequence rules and a response to the action on the merits which follows.

The aforementioned instance of failure to comply is not intended as an exhaustive list of all such potential failures to comply in the instant application. Applicants are encouraged to thoroughly review the application to ensure that the entire application is in full compliance with all sequence rules. This requirement will not be held in abeyance.

Claim Objections

Claims 18-54, 64 and 65 are objected to because of the following informalities: The word "deoxyribonucleotide" is spelled "deoxyribonuleotide" in claim 18. Appropriate correction is required. Claims 19-54, 64 and 65 are objected to because they depend from claim 18.

Claim 22 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 64 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 64 recites the limitation "the microRNA" in claim 18. However, claim 18 does not recite a microRNA. There is insufficient antecedent basis for this limitation in the claim. Claim 65 is rejected because it depends from claim 64.

Claim Rejections - 35 USC § 102 or 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18, 23-29, 34, 35, 39-54, 64 and 65 are rejected under 35 U.S.C. 102(e) or 35 USC 103(a) as being anticipated by or obvious over Khvorova et al. (US 2007/0039072 A1).

The instant claims are directed to a single stranded anti-microRNA molecule wherein at least ten contiguous bases have a sequence complementary to a contiguous sequence of bases in SEQ ID NO: 1, except that up to thirty percent of the base pairs may be wobble base pairs and up to 10% of the contiguous bases may be additions, deletions, mismatches, or combinations thereof, no more than fifty percent of the contiguous moieties contain DNA backbone units and the molecule is capable of inhibiting microRNP activity. The invention is further drawn to modifications of the molecule.

Khvorova et al. teach inhibitory RNA molecules that can be single or double-stranded (see page 5, for example) and specifically teach a single stranded RNA sequence that is 19 nucleotides in length that can form a Watson-Crick base pair with a complementary base and has ten contiguous bases that have a sequence complementary to a contiguous sequence of bases in instant SEQ ID NO: 1 except that three of the bases are wobble bases or mismatches. Nucleotides 2-11 (underlined) of SEQ ID NO: 303250 of Khvorova et al. (cacgagagccgcaccaaca) are complementary to nucleotides 11-20 of instant SEQ ID NO: 1, except for three nucleotides that are wobble or mismatches, meeting the instant claim limitations.

Khvorova et al. teach that the nucleotides can be RNA or DNA or modified forms of either. Khvorova et al. teach that the modifications can protect the compounds from degradation by nucleases and include phosphorothioates, amidates, 2'-sugar modifications such as 2'-O-methyls, peptides, 2'-halogens, chimeric compounds with RNA and DNA residues, individually or in combination. The modifications can be at any nucleotide position. Any terminal modification is considered to meet the instant limitation of "terminal cap", as the instant specification does not define this term and it is not a term of the art. The molecules of Khvorova et al. are designed to target human genes.

The instant specification does not define "anti-microRNA". The antisense RNA molecule of Khvorova et al. meets all of the structural limitations of the instant claims and is therefore considered to meet the instant limitation of an "anti-microRNA" molecule that is "capable of inhibiting microRNP activity" as instantly claimed, absent

evidence to the contrary. See, for example, MPEP § 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. 'There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102.' In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims."

Therefore, the instant invention is anticipated or obvious over Khvorova et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18-21, 23-54, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khvorova et al. (US 2007/0039072 A1), as explained in the rejection under 35 U.S.C. 102(e) above, in view of Kurreck (Eur. J. Biochem., 2003, 270, pages 1628-1644).

The instant claims are directed to a single stranded anti-microRNA molecule wherein at least ten contiguous bases have a sequence complementary to a contiguous sequence of bases in SEQ ID NO: 1, except that up to thirty percent of the base pairs may be wobble base pairs and up to 10% of the contiguous bases may be additions, deletions, mismatches, or combinations thereof, no more than fifty percent of the contiguous moieties contain DNA backbone units and the molecule is capable of inhibiting microRNP activity. The invention is further drawn to modifications of the molecule.

Khvorova et al. teach inhibitory RNA molecules that can be single or double-stranded (see page 5, for example) and specifically teach a single stranded RNA sequence that is 19 nucleotides in length that can form a Watson-Crick base pair with a complementary base and has ten contiguous bases that have a sequence complementary to a contiguous sequence of bases in instant SEQ ID NO: 1 except that three of the bases are wobble bases or mismatches. Nucleotides 2-11 (underlined) of SEQ ID NO: 303250 of Khvorova et al. (cacgagagccgcaccaaca) are complementary to nucleotides 11-20 of instant SEQ ID NO: 1, except for three nucleotides that are wobble or mismatches, meeting the instant claim limitations.

Khvorova et al. teach that the nucleotides can be RNA or DNA or modified forms of either. Khvorova et al. teach that the modifications can protect the compounds from degradation by nucleases and include phosphorothioates, amidates, 2'-sugar modifications such as 2'-O-methyls, peptides, 2'-halogens, chimeric compounds with RNA and DNA residues, individually or in combination. The modifications can be at any

nucleotide position. Any terminal modification is considered to meet the instant limitation of "terminal cap", as the instant specification does not define this term and it is not a term of the art. The molecules of Khvorova et al. are designed to target human genes. Khvorova et al. teach that there need not be 100% complementarity between the antisense sequence and that target sequence and therefore mismatches throughout the sequence are considered obvious.

The instant specification does not define "anti-microRNA". The antisense RNA molecule of Khvorova et al. meets all of the structural limitations of the instant claims and is therefore considered to meet the instant limitation of an "anti-microRNA" molecule that is "capable of inhibiting microRNP activity" as instantly claimed, absent evidence to the contrary.

Although Khvorova et al. do teach certain chemical modifications, Khvorova et al. do not teach methoxyethyl modifications, methylene bridges, morpholino phosphoroamidates, tricyclo or cyclohexane nucleotides.

Kurreck teaches various modifications for antisense agents that stabilize the agents against nucleolytic degradation and enhance their target affinity. Kurreck teaches that alkyl modifications at the 2' position enhance the activity of antisense agents. For example, Kurreck teaches chimeras, 2'-O-Methyls, 2'-O-methoxyethyls, PNAs, morpholino phosphoroamidates, cyclohexane nucleic acids, tricycle nucleic acids, and LNAs with methylene bridges. Kurreck teaches that single stranded antisense oligonucleotide and siRNA molecules have challenges, such as the need to be protected against nucleolytic attack.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate each of the modifications taught by Kurreck into the compound of Khvorova et al.

One would have been motivated to incorporate each of the modifications taught by Kurreck into the compound of Khvorova et al. because Kurreck teaches that the modifications each enhance the activity of antisense agents by stabilizing the agents against nucleolytic degradation, which is the same reason that Khvorova had incorporated modifications. Furthermore, Kurreck teaches that siRNA molecules and single stranded antisense oligonucleotides are each antisense agents that need to be protected against nucleolytic attack.

Finally, one would have a reasonable expectation of success given that Kurreck and Khvorova et al. each teach chemical modifications and each teach that such modifications add stability against nucleolytic degradation. Therefore, one would reasonably expect for the modifications of Kurreck to add the same benefit to the compounds of Khvorova et al.

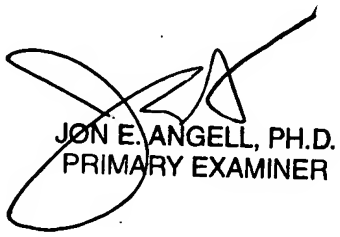
Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is (571) 272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Amy H Bowman
Examiner
Art Unit 1635

AHB